The second case illustrates a complication of which other observers[9] have warned. In this case, a simple kink in the tube most likely was at fault. As in the preceding case, air could be inserted into the cuff under greater-than-usual pressure, and again the pilot balloon proved misleading.

Ultimately the fault in each case lay in defects of the inflating tube. Preventing these complications can be achieved by one or more of the following measures: (1) Placing the clamp which secures cuff-pressure over the inflating tube between the pilot balloon and the orifice of the inflating tube; (2) Using an air-tight check (usually via a "disposable" plastic syringe) on the exact amount of air inserted into, and then removed from, the cuff; or (3) Using no clamp and leaving an air-tight syringe attached to the inflating tube, the proper pressure being maintained by taping the plunger to the barrel at the appropriate level; or (4) Using the technique recommended by Martinez[7] in which the same intermittent air pressure which ventilates the patient intermittently inflates the tracheal tube. The latter technique is under development.

Summary

Two cases—one fatal—of complications in the use of tracheal cuffs are presented. In both cases the difficulty was due to hyperinflation of the cuff (one an orotracheal cuff, the other a standard tracheostomy cuff) due to malfunction of the inflating tube. Corrective and preventive measures are mentioned.

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Ethanol-Induced Hypoglycemia

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CASES OF HYPOGLYCEMIA occurring after ethanol ingestion have been reported frequently in recent years. As experience has accumulated, it has been found that a period of fasting occurs before the hypoglycemic reaction. In many of the reports the patient was first seen in coma of unknown cause.

Most current reviews of coma neglect this entity; and the frequent association of alcoholism with epileptic seizures, hepatic failure, cerebrovascular accidents, head trauma, hypertensive encephalopathic states and delirium tremens tends to obscure the possibility of ethanol-induced hypoglycemic coma. The following case is being presented to stress again the association of hypoglycemia and previous heavy drinking.

Report of a Case

A 42-year-old Negro man had been arrested for intoxication and booked at the city jail several hours before his admission to hospital. While in jail he reportedly had a seizure, injured his head and was brought semi-comatose to the emergency room. He had a history of 20 years of alcoholism with recent excessive intake of tokay wine. He had had previous admissions, for head trauma and for pneumonia. There was no history of seizures.

On physical examination he responded only to painful stimuli by moving all extremities, all equally well. Rectal temperature was 99°F. Except for a slightly wasted appearance, a small abrasion at the left occiput, occasional symmetrically tonic movements of the limbs, bilateral Babinski reflexes and hyperactive deep tendon reflexes, the results of examination were within normal limits.

After an initial specimen of blood was drawn for determination of sugar content (which was later reported to be 17 mg per 100 ml), 50 ml of 50 per cent glucose solution was administered intravenously. Over the subsequent five minutes

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the patient became alert and oriented and neurologically normal.

X-ray films of the skull, abdomen and chest were normal. An upper gastrointestinal tract series showed a deformed duodenal bulb. An electrocardiogram revealed normal sinus rhythm, high voltage with SV_1 plus RV_5 of 37 mm, QS waves in leads II, III and a VF, inverted T waves in leads I and a VL and depressed T waves in leads V_{5-6}. The hematocrit was 40 per cent. Leukocytes numbered 6,700 per cu mm with 58 per cent neutrophils, 38 per cent lymphocytes, 3 per cent eosinophils and 1 per cent basophiles. Urea nitrogen was 13 mg per 100 ml. The icteric index was 6 units; bromosulfalein retention was 4 per cent at 45 minutes; prothrombin concentration was 100 per cent; thymol turbidity was 3.5 units; cephalin flocculation was negative; and total serum protein was 8.60 gm per 100 ml with albumin of 4.34 gm and globulin of 4.26 gm. Urinalysis revealed a trace of protein, absence of sugar and 3 to 4 white blood cells per high power field. Liver biopsy was reported as normal. On lumbar puncture, no abnormalities of the cerebrospinal fluid were noted.

In order to rule out the usual causes of hypoglycemia the following tests were performed: After three days on a 2,800 calorie, 285 gm carbohydrate diet, an oral glucose tolerance test was done with 100 gm of glucose. The result was interpreted as normal.

An intravenous tolbutamide test was next done by infusing intravenously 1 gm of sodium tolbutamide over five minutes. This resulted in a fall of blood sugar from 92 mg per 100 ml to 54 mg at one hour and a return to 69 mg by three hours. This was followed by a 72-hour fast terminated by one hour of vigorous exercise and 2 mg of glucagon injected subcutaneously. This caused a slight fall in blood sugar level with fasting, followed by a rise of 20 mg per 100 ml after glucagon administration and a slow decline after one hour.

In a non-fasting state, the patient ingested 50 ml of 95 per cent ethanol. Blood sugar determinations began with a fasting level of 106 mg per 100 ml and decreased slowly to 86 mg after six hours.

Finally, a fasting ethanol ingestion test was performed by administering 50 ml of 95 per cent ethanol at 61 hours and again at 66 hours of fasting. This test was terminated at 68.5 hours because of a hypoglycemic reaction with blood sugar of 33 mg per 100 ml.

Discussion

Brown and Harvey[2] first associated hypoglycemia with ingestion of denatured alcohols in 1941. They concluded the hypoglycemia was caused by a non-ethanolic ingredient found in these alcohols. However, their attempts to reproduce the hypoglycemia in animals failed.

In 1961, Neame and Joubert[10] described several cases of postalcoholic hypoglycemia associated with mild, transient toxic hepatitis. This hypoglycemia occurred commonly 12 hours after the ingestion of excessive ethanol, but occasionally would not manifest itself for a day or more.

Subsequently there have been several reports of ethanol-induced hypoglycemia and many unproven theories have been advanced as to the biochemical mechanisms involved. Recently Freinkel[7] and Field[5] showed that it is possible to induce hypoglycemia in normal persons as well as in addicts to alcohol merely by preceding the ethanol ingestion with a fasting period. A period of 48 to 72 hours is usually required; however, subjects with marginal hepatic glycogen stores may require only overnight fasts.[6]

Manifestations

The bizarre manifestations of hypoglycemia and common association of alcohol intoxication with the varied causes of coma may obscure the diagnosis. A history of recent poor caloric intake associated with ethanol ingestion would be helpful but is virtually never offered by the patient. Fewer than half of all reported cases have occurred in alcoholics.[5]

Frequently there are no signs of the expected adrenergic reaction to hypoglycemia as is seen during a rapid decrease in blood sugar.[3,8] Instead, only a cerebral reaction occurs, due to a slow decline in blood sugar to profoundly low levels. Because of this, in all reported cases the patients were in semi-coma or deep coma with blood sugar ranging between 12 and 47 mg per 100 ml.[2,8,10] Hypopyrexia—95° to 97°F—has been frequently reported. Findings on neurological examination often are inconsistent. The deep tendon reflexes may be increased or decreased. Vital signs are usually depressed. There may be seizures, generalized tremor and conjugate deviation of the eyes.

Since these varied manifestations tend to obscure the real diagnosis, the possibility of hypoglycemic coma must be raised on the basis of association. It is possible that if the diagnosis is not

considered the patient may continue in coma until death or irreparable brain damage occurs.

Differential Diagnosis and Diagnostic Steps

The differential considerations in the diagnosis of hypoglycemia are many and the reader is referred to the standard medical texts. An insulinoma is the most difficult to differentiate, because the intravenous tolbutamide tolerance test when given to an alcoholic after prolonged poor intake of food frequently results in a sustained hypoglycemia simulating the prolonged reaction typically seen with an insulin-secreting tumor of the pancreas.[9] In all other causes of hypoglycemia there is transient hypoglycemia (30 to 40 minutes) followed by a return to normal over an hour and a half to three hours.[4] In the case here reported the blood sugar was normal within three hours.

An insulinoma will usually cause hypoglycemia during a two-day fast. Frequently, however, blood sugar remains normal during this period and decreases only after provocation with vigorous exercise.[3] In the present case the patient fasted for two days and then walked vigorously for an hour without effect. This exercise period was followed by a subcutaneous injection of 2 mg glucagon and the response was subnormal, showing that there was a decrease in hepatic glycogen stores. The hypoglycemia induced by ethanol is always refractory to glucagon.[1]

A standard oral glucose tolerance test after three days of carbohydrate loading is adequate to rule out diabetes mellitus and the functional causes of hypoglycemia. With hepatic disease, this test usually reveals a plateau in the glucose tolerance curve, and other evidence of liver disease is also present. In the case presented, the results of the glucose tolerance test as well as all measurements of hepatic function and a liver biopsy were within normal limits.

If there is evidence of other causes of hypoglycemia such as adenohypophyseal and adrenocortical hypofunction, sarcomata, fibromata and central nervous system disease, these possibilities must be eliminated by appropriate tests.

After all abnormal causes of hypoglycemia have been eliminated, the duplication of the clinical situation by fast and ethanol ingestion may be attempted. After fasting for 68.5 hours and ingesting 100 ml of 95 per cent ethanol, the patient in the present case became confused and diaphoretic, and the blood sugar was 33 mg per 100 ml.

Mechanisms

Past explanations of the mechanism of hypoglycemia have all been inadequate. A simple explanation is lacking. Recent work suggests that ethanol produces hypoglycemia by inhibiting gluconeogenesis and hepatic glycogen synthesis.[1,5] When ethanol is metabolized, it causes changes in co-enzyme systems, resulting in a disturbance of enzymatic control of carbohydrate metabolism. This disturbance causes further glycogen depletion which in turn increases the vulnerability of the liver to the effects of ethanol. This cycle persists until it is broken by the administration of carbohydrate.[7]

Summary

In the case of a 42-year-old Negro man who was in hypoglycemic semi-coma when first seen, the condition was found to be due to ethanol ingestion. Such hypoglycemic reactions are caused by the association of fasting and ethanol ingestion and show varied manifestations. Usually the only suggestion of this state is the association of coma with alcohol and perhaps hypopyrexia. Glucose administration and adequate feeding usually results in complete recovery.

The mechanisms of ethanol induced hypoglycemia remains speculative. Recent studies, however, suggest an ethanol inhibition of gluconeogenesis and hepatic glycogen synthesis.

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